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Fried, well-done red meat and risk of lung cancer in women (United States)

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Objective: **Some epidemiological studies suggest that diets high in fat, saturated fat, or cholesterol are associated with increased risk of lung cancer. Since meat consumption is correlated with the intake of saturated fat and cholesterol, we investigated the role of meat intake and cooking practices in relation to lung cancer risk.**
Methods: **A population-based case-control study of both non-smoking and smoking women was conducted in Missouri. A 100-item food frequency questionnaire (FFQ) with detailed questions on meat consumption was completed by 593 cases and 623 frequency matched controls. We estimated quantity of meat eaten (grams/day) according to cooking method, and doneness level. Odds ratios (ORs) and 95% confidence intervals (C.I.s) were calculated using logistic regression. Multivariate models included age, packyears of smoking, body mass index (BMI, kg/m^2), education, and intake of calories, fat, fruit/fruit juices, and vegetables.**
Results: **When comparing 90th and 10th percentiles, lung cancer risk increased for total meat consumption (OR = 1.6, C.I. 1.1-2.4), red meat (OR = 1.8, C.I., 1.2-2.7), well-done red meat (OR = 1.5, C.I.s, 1.1-2.1) and fried red meat (OR = 1.5, C.I., 1.1-2.0). The odds ratios for 5th vs. 1st quintiles using the categorical variable for well-done red meat and fried red meat were essentially the same as reported above; however, the increase in risk was associated mainly with the 5th quintile. The ORs for a 10-gram increase in consumption were, 1.04 for total meat, 1.06 for red meat, 1.08 for well done red meat, and 1.09 for fried red meat.**
Conclusions: **Consumption of red meat, especially fried and/or well-done red meat, was associated with increased risk of lung cancer.** *Cancer Causes and Control*, 1998, **9**, 621-630

Key words: Cooking methods, heterocyclic amines, lung cancer, red meat.

Background

Since several epidemiologic studies suggest that lung cancer risk may be associated with intake of cholesterol, total and saturated fat,[1-6] we investigated the role of meat intake as a correlate of dietary fat. We also evaluated the role of meat cooking practices in the etiology of the disease. Few studies have examined the role of meat cooking and risk of lung cancer. In a Swedish study,[7] lung cancer risk was not associated with consumption of meat or fish cooked and preserved by various methods. In contrast, a study from Uruguay[8] found increased risk with higher consumption of fried meat. Consumption of well-done, well-browned meat has been associated with increased risk of cancer of various sites.[9-13] Well-done meat has been assumed to be a surrogate of exposure to heterocyclic amines but evidence of carcinogenicity of these compounds in humans is not conclusive.[14]

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In a population based case-control study of lung cancer, we obtained detailed information on meat cooked by different methods to varying degrees of doneness to evaluate the role of meat and cooking practices on lung cancer risk.

Materials and methods

Cases

Of 783 women, mostly former and current smokers, with primary lung cancer reported to the Missouri Cancer Registry between January 1, 1993, and January 31, 1994, 41 women were not eligible for this study (7 were not Missouri residents and 34 did not have primary lung cancer). Of the 742 remaining cases, 697 women or a proxy participated in a brief telephone interview (13 subject refusals; 13 physician refusals; and 19 cases with no suitable proxy respondents). An additional 32 cases under age 65 without driver's license at the time of diagnosis were not eligible, since controls under 65 were identified through the Missouri drivers' license registry. Of the 665 remaining cases, 610 agreed to an in-person dietary interview. Sixteen subjects were excluded from the analysis because of implausible dietary information (*e.g.* too few items consumed in a day) and one woman did not respond to the meat cooking method section of the FFQ. Eighty four percent of eligible cases were used in these analyses, that is 593 out of 710 (742 minus 32 without driver's license) with direct interviews (self-reporters) obtained from 358 cases out of 593 (60 percent).

Controls

For women between the ages 30-64, names and addresses were randomly selected from drivers' license files. For women between the ages of 65-84 years, names and addresses were randomly selected from lists provided by the federal Health Care Financing Administration. These lists include an estimated 95 percent of the women in this age group.[15]

To facilitate efficient recruitment of controls and reduce analysis constraints, we used probability matching.[16] The procedure involved a two-stage randomized recruitment process,[17] described in an earlier publication,[18] and was used primarily to avoid the expected imbalance in smoking status of cases versus controls. The two groups were recruited simultaneously. Briefly, in selecting controls, the goal was to over represent vulnerable individuals (*i.e.*, smokers) to the same extent that they would be over represented in the case series. This procedure required prior information of estimates of disease rates or odds ratios associated with each category of smoking.

From computer records of the 1993 Missouri cancer registry, among women we found approximately 9 percent of lung cancer cases were lifetime nonsmokers, 26 percent stopped smoking three or more years ago (previous smokers), 45 percent smoked less than 30 cigarettes per day (light-to-moderate smokers), and 20 percent smoked 30 or more cigarettes per day (heavy smokers). The disease rates according to smoking status were used to develop the sampling probabilities to select controls from the larger pool of 3,386 eligible women. The randomization procedure was established separately for Whites and other races combined and was based on the four smoking status categories.

Potential controls also were frequency matched to cases using 5-year age strata. All heavy smokers in the pool of potential controls among Whites and non-Whites were invited to participate (*i.e.*, sampling probability of one). Sixty-two percent of White light smokers (75 percent of non-Whites), 26 percent of White former smokers (34 percent of non-Whites) and 4 percent of White nonsmokers (6 percent of non-Whites) were invited to complete an entire interview.

Screening interviews were attempted on a total of 4,592 potential controls with telephones numbers and/or complete address information. For the 3,386 controls that were found to be eligible by screening criteria, 730 subjects were selected, 700 completed the interview, and 628 (86 per cent of eligible controls that were selected) provided information on diet, meat cooking practices, and relevant potential confounding exposures. We excluded 4 control subjects due to implausible dietary information, and one for missing data for meat cooking practices. The final number of controls used in the analyses is 623 out of 730 (85%) of which 617 out of 623 were interviewed directly (99%).

Food frequency questionnaire and meat cooking methods module

The methods used for dietary assessment are described in detail elsewhere.[19] Briefly, a modified version of the 100-item Health Habits and History Questionnaire was used to obtain information on usual diet (frequency of consumption and portion size) approximately 2-3 years prior to diagnosis. The 100-item questionnaire was modified to more accurately assess fat intake and to provide more detailed assessment of vegetable consumption.

Two sections of the questionnaire were used to obtain details on meat consumption and cooking patterns. In the first part of the dietary questionnaire, information on consumption frequency and portion size was obtained for 22 meat and fish items (Appendix I). Of these, 15 were red meat items (one person reported eating lamb in the 'open-ended' section of the questionnaire as an add on item). In another part of the questionnaire we obtained information on cooking methods and doneness levels of 7 red meat items (Appendix II): hamburger/cheeseburger, beef roast, beef steak, pork chops/ham steaks, hot-dog/sausage, bacon, and breakfast sausage. For example, if someone reported consuming hamburger, they were asked to indicate one method of cooking (pan-fried, oven-broiled, grilled/barbecued, microwaved, or other) and one level of doneness (rare, medium-rare, medium, medium-well, well done, very well done) to describe usual preparation methods. See Appendix II for the cooking methods and doneness levels included in the questionnaire for each meat item. We did not ask about methods of preparation or doneness for the other 8 red meat items as they were assumed to be cooked in a more uniform manner.

Calculation of daily grams of meat consumed

We estimated the quantity of each type of meat eaten (grams/day) by multiplying the frequency of consumption and portion size. For the 7 items which included questions about method of preparation, we could also estimate grams of meat consumed according to cooking method and doneness level. For example, to calculate grams of fried meat consumed we added up grams of the seven types of meat for which pan-frying was the most common way of cooking. For doneness level, we created two different categories: 'well done' and 'not well done'. To calculate the amount of meat in the 'well done' category we added grams of well done and very well done steak, hamburger, and beef roast; very well done/crisp, and charred hot-dog or sausage; well done/crisp bacon and breakfast sausage; and very well done pork chops and ham steaks. To derive the 'not well done' variable we calculated gram amounts of the above items cooked medium or rare.

For subjects with missing data on cooking practices for a particular meat, the doneness level was imputed using the median value of controls, while the cooking method was imputed using the most common choice among controls. The imputed values were as follows: hamburger patties-pan-fried, well done; steak — grill/barbecue, well done; pork chop — pan-fried, well done; fried chicken — pan-fried; non-fried chicken — baked, well done; bacon-pan-fried, very well done; sausage-pan-fried, very well done. No imputations were necessary for 86 percent of the subjects, 11 percent had one imputation, 2 percent had 2, and less than 1 percent had more than two imputations for the 7 red meats used in the analyses.

Statistics

For the statistical analysis we used logistic regression[20] for meat variables (continuous) reflecting the estimated average quantity in grams eaten per day. All analyses were adjusted for age, packyears of smoking, body mass index (BMI, kg/m^2), calories, fat, fruit/fruit juices and vegetables, using continuous variables, and education using a categorical variable (<12 years, 12 years, and >12 years) as confounders.

Odds ratios were calculated using a fitted logistic regression model, taking the ratio of the estimated odds at two different gram consumption levels, the medians of the 5th and 1st quintiles (*i.e.* the 90th and 10th percentiles) based on the controls. The 95 percent confidence intervals are given for these odds ratios. To test for trend, we determined if the fitted logistic regression parameters were significantly different from zero. The trend was considered significant at the 0.05 level and if the 95 percent confidence interval did not contain 1. The odds ratios of the quintiles using categorical variables were also examined.

Odds ratios for one type of meat cannot be directly compared to another if the median levels of consumption in the upper and lower quintiles are very different for various subsets of meat. If such a comparison were done, the two sets of risk estimates would only reflect differences in consumption levels. In order to enable comparisons among different types of meats, we present a second set of odds ratios, reflecting the relative risk associated with an increased consumption of 10 grams. Because of the linearity of the logistic regression model, these odds ratios are the same whether we are comparing 10 verses 0 grams or 100 verses 90 grams of consumption. These odds ratios are by nature small since they reflect a change in consumption of only 10 grams. Furthermore, as they are derived from the same logistic regression model as the other odds ratio with simple rescaling, the two are either both significantly different from 1, or neither of them are.

For possible comparisons with future studies, reporting odds ratios using different gram amounts, it can be noted that the odds ratio for a difference of x grams, OR(x), is equal to $[OR(10)]^{x/10}$. In this manner, the use of the original continuous as opposed to categorized variables facilitates the comparison of odds ratio estimates among studies.

For this particular data set, the continuous model also fits better than a categorical model based on quintiles of the meat variables, even though the latter have three additional degrees of freedom. We also checked for non-linearity by adding a quadratic term to the continuous model. In no case was this term statistically significant, and thus was left out of the final logistic regression model. This does not necessarily mean that the true relation is a linear one but the current sample size is not enough to establish the shape of a non-linear risk functions, unless the non-linearity is very strong.

We attempted to disentangle the effects of red meat intake from method of preparation. For an addition effect, we examined a 10-gram change in well done meat consumption, holding the consumption of not-well done meat constant. If instead we looked at a substitution effect, then a 10-gram change in well-done red meat was compensated by the opposite change for not-well done red meat, holding the total red meat consumption constant.

Results

The mean age of both cases and controls was 66 years. The controls had a higher level of education and greater BMI, smoked less, consumed slightly fewer calories and fat but more fruits and vegetables (Table 1).

The mean intake of different types of meat consumed by cases and controls is presented in Table 2. The average total meat intake was 108 grams per day for the controls and 117 grams per day for the cases. However, the higher meat consumption (8.2 percent total meat and 13.2 percent red meat) by cases cannot be explained solely by total calorie intake which was only 4.9 percent greater in cases. Over two-thirds of the total meat consumed was red meat (beef and pork) and hamburger patties were the most commonly consumed individual meat item among both cases and controls.

Frequency distribution of intake of total meat, red meat, the seven items of red meat with information on cooking methods, and well-done red meat is presented in Figure 1 for all subjects. Total meat and red meat intakes are nearly normally distributed. As we examine subsets of these meat groups the distributions are more skewed and nearly exponential for well done meat.

Table 1. Potential risk factor characteristics of case and control subjects

	Cases	Controls
	Mean (10th and 90th percentile)	Mean (10th and 90th percentile)
Total number	593	623
Age (years)	66 (52, 68)	66 (52, 79)
Education (%)		
<12 years	36.3	26.0
=12 years	44.4	46.4
>12 years	19.3	27.6
Pack years	48 (6, 95)	30 (0, 64)
BMI	24 (19, 31)	25 (20, 32)
Energy (Kcal/day, excluding alcohol)	1638 (904, 2490)	1562 (921, 2358)
Fat (g/day)	75 (36, 122)	70 (34, 112)
Fruit and fruit juices (g/day)	172 (25, 341)	200 (30, 381)
Vegetables (g/day)	16 (3, 32)	20 (4, 40)

Thus, if we analyze the subsets of these meat groups categorically there would be little difference in the lower quantiles while the upper quantile would contain a large range of intake.

Adjusted risk estimates for lung cancer with various types of meat, doneness level, and cooking method are shown in Table 3, for all subjects (self-reporters and proxies) as well as for self-reporters only. In the analysis with all subjects, a significant increased risk of 1.6, C.I.s, 1.1-2.4 (90th vs. 10th percentile of meat consumption among controls) was observed for total meat consumption (simple model). When total meat intake was divided into red meat and white meat, an increased risk of 1.8, C.I.s, 1.2-2.7, was associated with red meat while there was no significant effect of white meat (red/white meat model). When the analyses were restricted to self-respondents, the risks for total meat and red meat consumption were still elevated (1.5, C.I.s 1.0-2.4) but no longer statistically significant.

We observed increased risk associated both with doneness level (doneness model) and cooking methods (cooking method model) of red meat (Table 3). Risk was significantly elevated for well-done meat consumption for all subjects (1.5, C.I.s, 1.1-2.1) as well as for self-reporters only (1.5, C.I.s, 1.0-2.1). Similarly, an increased risk (1.5, C.I.s, 1.1-2.0) was associated with higher intake of fried red meat. The increased risk for self-reporters was lower but remained statistically significant (1.4, C.I.s, 1.0-1.9). The odds ratios for 5th vs. 1st quantiles using the categorical variable were essentially the same as reported above, however, the increase in risk was associated mainly with the 5th quantile.

As shown in Table 3, each 10 gram increment corresponds to a 4 percent increase in risk (OR = 1.04) for total meat, 6 percent (OR = 1.06) for total red meat, and 8 percent OR = 1.08) for well done red meat. The latter may be compared to 2 percent increase (OR = 1.02) for not well-done red meat. The risk associated with 10 gram increase in fried red meat was 9 percent (OR = 1.09) for all subjects. Microwaving red meat was found to be protective (0.8, C.I.s,. 0.6-0.9) in the analysis of all subjects. For total other red meat, *i.e.* for meat types with no doneness information (meat items 8-16, in Table 2), there was a significant elevated risk with an odds ratio of 1.08 for each additional 10 grams consumed.

When we attempted to disentangle the effects of red meat intake from method of preparation, the odds ratio for the addition effect is 1.08 per 10 gram of well-done meat. If instead we look at a substitution effect we have an odds ratio of 1.06. This result is no longer statistically significant (C.I.s, 0.99-1.12), which means that although the significant result for red meat is driven by well-done red meat rather than not-well done red meat, we cannot separate these two effects to say that one is significant

Table 2. Amount of different types of meat consumed by cases and controls

Type of meat	Grams of meat consumed per day by cases (n = 593). Mean (10th and 90th percentile)	Grams of meat consumed per day by controls (n = 623). Mean (10th and 90th percentile)
All meats	116.7 (52.2, 201.5)	107.9 (46.3, 172.9)
Red meat (includes 1 to 15)	82.1 (30.9, 147.8)	72.5 (23.9, 127.8)
Red meat with cooking information (1 to 7)	54.6 (16.4, 102.1)	48.3 (13.9, 91.1)
1. Hamburger patty	22.4 (1.9, 56.7)	19.1 (1.4, 29.9)
2. Beef roast	7.6 (1.0, 17.0)	7.3 (1.0, 17.0)
3. Steak	6.7 (0, 17.0)	6.4 (0, 17.0)
4. Pork chops	5.5 (0, 16.8)	4.5 (0, 10.8)
5. Hot-dogs	4.9 (0, 17.6)	4.7 (0, 17.6)
6. Sausage	3.9 (0, 10.8)	3.5 (0, 10.8)
7. Bacon	3.4 (0.1, 8.0)	2.8 (0, 6.9)
Red meat without cooking information (8 to 15)	27.5 (7.1, 57.5)	24.3 (6.1, 47.3)
8. Luncheon meat	9.4 (0, 24.3)	7.1 (0, 20.5)
9. Other ground beef	8.0 (0, 16.8)	8.0 (0.8, 16.8)
10. Pork roast	2.6 (0, 1.4)	2.2 (0, 6.9)
11. Spaghetti sauce with meat	2.3 (0.3, 5.6)	2.5 (0.3, 5.6)
12. Liver	2.2 (0, 6.6)	1.9 (0, 5.8)
13. Liverwurst	2.2 (0, 1.9)	1.9 (0, 1.4)
14. Beef stew	2.1 (0, 4.7)	1.9 (0, 5.0)
15. Lamb	0.03 (0, 0)	0 (0, 0)
Well-done red meat (1-7)	31.6 (2.9, 68.9)	25.9 (1.6, 57.5)
Not-well done red meat (1-7)	23.0 (1.4, 58.8)	22.4 (0.7, 51.1)
Fried red meat (1-7)	25.3 (1.2, 58.3)	19.5 (0, 47.6)
Grilled red meat (1-7)	12.3 (0, 36.9)	12.0 (0, 35.4)
Baked/Roasted red meat (1-7)	8.0 (0.8, 17.0)	7.5 (0, 17.0)
Broiled red meat (1-7)	3.7 (0, 12.5)	3.4 (0, 12.9)
Microwaved red meat (1-7)	1.5 (0, 5.0)	2.3 (0, 7.3)
Other method of cooking (1-7)	3.8 (0, 10.5)	3.4 (0, 8.8)
White meat	34.6 (10.5, 66.7)	35.4 (10.8, 66.3)
Chicken	17.4 (3.1, 32.6)	17.9 (3.4, 35.5)
Fish and other sea food	17.2 (3.1, 35.5)	17.5 (2.5, 35.6)

after adjusting for the other as we do not have enough power. We obtain similar results with fried meat where the odds ratio is 1.09 for the addition of 10 grams of fried meat holding non-fried red meat constant, but for the substituting effect the odds ratio decreases to 1.06 (C.I.s, 0.99-1.13).

There was no correlation of cigarette smoking and meat cooking preference. The nonparametric Spearman correlation coefficients are 0.09 ($p = 0.003$) for pack-years and total red meat of types 1-16; −0.01 ($p = 0.63$) for packyears and the proportion of well-done meat in relation to total red meat of types 1-7, and 0.05 ($p = 0.07$) for packyears and the proportion of fried meat in relation to total red meat of types 1-7. The risk associated with the red meat intake, doneness level and cooking technique did not change when smoking status (never/ever/current) and years-quit-smoking was included in the model together with cumulative exposure (pack years).

We performed an exploratory analyses on the individual 7 red meat items for which we had information on doneness. A statistically significant result was observed for well-done hamburgers with an OR of 1.11 (C.I.s, 1.04-1.20), associated with a 10-gram increase in consumption. There was an increased risk observed for pork chops and ham steaks with an OR of 1.27 (C.I.s, 1.00-1.62) and an OR of 1.26 (C.I.s, 0.88-1.82) for well-done and very-well done chops, respectively. Only the former was significant due to the larger number of subjects in that category.

In another exploratory analysis we examined each red meat individually. Here we present these data as odds ratios using the 90th vs. 10th percentile of meat consumption among controls rather than increase per 10 gram meat consumption as for many of these meats types 10 gram consumption would be unlikely. Luncheon meat (1.5, C.I.s, 1.1-2.1), pork chops and pork steaks (1.4, C.I.s, 1.0-1.9) and beef stew (1.3, C.I.s, 1.0-

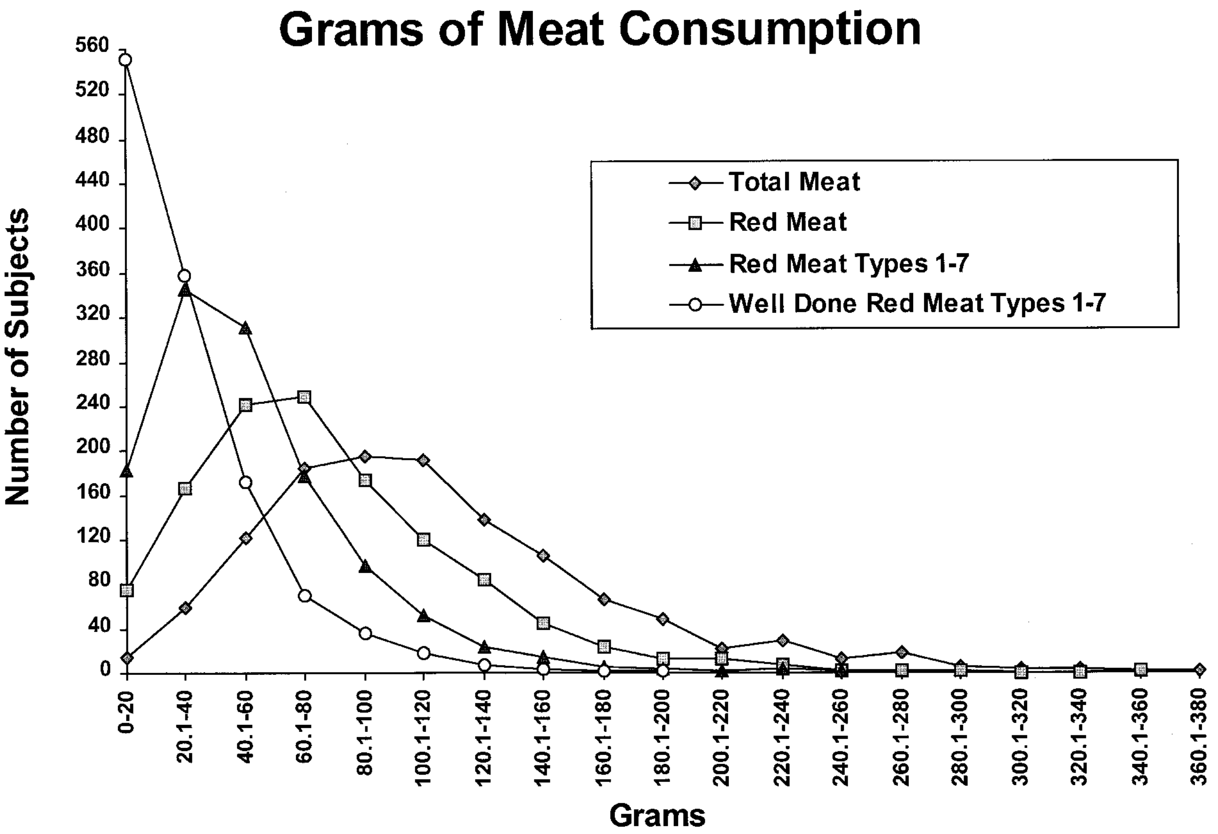

Figure 1. Distribution of various subgroups of meat intake. Red meat 1-7 (see Appendix I) are the red meats with information on doneness level.

Table 3. Relative risk associated with meat intake and meat doneness and cooking method

	All subjects		Self reporters	
	OR (C.I.s) (10th vs. 90th percentile of meat consumption among controls)	**OR for 10 gram increment difference**	**OR (C.I.s) (10th vs. 90th percentile of meat consumption among controls)**	**OR for 10 gram increment difference**
Simple model				
All meat	1.6 (1.1, 2.4)*	1.04*	1.6 (1.0, 2.5)	1.04
Red/white meat model				
Red meat (1-15)	1.8 (1.2, 2.7)*	1.06*	1.5 (1.0, 2.4)	1.04
White meat	1.0 (0.7, 1.5)	1.01	1.2 (0.8, 1.8)	1.03
Doneness model				
Well-done red meat (1-7)	1.5 (1.1, 2.1)*	1.08*	1.5 (1.0, 2.1)*	1.07*
Not-well done red meat (1-7)	1.1 (0.8, 1.5)	1.02	1.1 (0.8, 1.5)	1.02
Other red meat (8-15)	1.4 (1.0, 2.0)*	1.08*	1.2 (0.8, 1.9)	1.04
Cooking method model				
Fried red meat (1-7)	1.5 (1.1, 2.0)*	1.09*	1.4 (1.0, 1.9)*	1.07*
Grilled red meat (1-7)	1.1 (1.0, 1.4)	1.03	1.1 (0.9, 1.4)	1.04
Broiled red meat (1-7)	1.2 (0.9, 1.5)	1.10	1.2 (1.0, 1.4)	1.12
Baked/Roasted red meat (1-7)	1.0 (0.8, 1.3)	0.99	0.9 (0.7, 1.3)	0.95
Microwaved red meat (1-7)	0.8 (0.6, 0.9)*	0.73*	0.8 (0.6, 1.00)	0.73
Other method of cooking (1-7)	1.0 (0.9, 1.2)	1.03	1.0 (0.8, 1.2)	0.97
Other red meat (8-15)	1.4 (1.0, 2.0)	1.08	1.2 (0.8, 1.8)	1.05

* Statistically significant at 0.05.
Adjusted for age, fat intake, calories, smoking (pack years), BMI, fruit and vegetable intake as continuous variables, education (<12 years, =12 years, >12 years) as categorical, as well as other meat variables listed in each model.
All subjects: 593 cases and 623 controls; Self reporters: 358 cases and 617 controls.

1.7) were found to significantly increase the risk of lung cancer.

Discussion

Lung cancer risk was higher among women who were frequent consumers of meat. However, the adverse effect of frequent meat consumption was no longer statistically significant after the data from the proxy respondents were removed. Women consuming well-done red meat or fried red meat had increased risk of lung cancer which remained statistically significant after removing the proxy respondents from the analyses.

Meats cooked at high temperatures produce various pyrolysis products depending on the cooking method used. A family of compounds known as heterocyclic amines (HCAs) is produced when meats are cooked at high temperatures, particularly pan-frying and grilling/barbecuing.[21-24] HCAs are formed when creatine and amino acids in meat juices pyrolyze. These compounds are highly mutagenic in Ames Salmonella tests and carcinogenic in animal studies.[25,26] Another group of compounds, polycyclic aromatic hydrocarbons (PAHs), is formed during grilling/barbecuing.[27] The fat drips on the heated surface, burns and the smoke carries the PAHs to the food surface. PAHs are established animal carcinogens.[27] Furthermore, meats cooked at high temperatures contain many more pyrolysis compounds (*e.g.*, well-done meat has many more peaks in high pressure liquid chromatography analyses than rare meat — personal observation) which in combination may be important in the carcinogenic process.

The two main factors that influence the production of these pyrolysis products are time and temperature.[28] Epidemiologists have tried to identify surrogates for these two factors. Doneness of meat or external browning may be a reasonable surrogate for cooking time and temperature. Well-done meat has been associated with increased risk of colon, breast and stomach cancers.[9-13] We are now reporting a possible association between lung cancer and well-done red meat with an increased risk of around 8 percent per 10 grams of well done/very well done red meat consumed.

Using cooking method as a surrogate for temperature, we found increased risk of lung cancer associated with fried red meat. There was an increased risk of approximately 9 percent for every 10 gram increase in consumption of fried red meat. Our results are similar to a study conducted by Deneo-Pellegrini in Uruguay[8] who found increased risk of lung cancer with higher consumption of all red meat, beef, and fried meat. In contrast, a study from Sweden[7] did not find increased risk in lung cancer with consumption of fried meat and meatballs. Associations of fried meat or fried foods with cancer in the breast, colon, pancreas, and stomach have been reported elsewhere.[9,10,12,14,29-34]

We also found increased risk of lung cancer associated with some red meats for which we had no cooking information. In exploratory analyses, luncheon meat and beef stew appeared to be associated with increased risk of lung cancer. Most luncheon meat contains either nitrates or nitrites, and smoked luncheon meat contain PAHs. However, this finding needs to be examined in a different study designed to appropriately test these hypotheses. The subjects in this study consumed very little beef stew. Further we did not have an a priori hypothesis for this association.

The role of meat in lung cancer risk is not clear, with some studies showing no association[7,35,36] while others find increased risk with higher red meat consumption.[1,19,37-40] From our data it appears there may be a small increase in risk of lung cancer associated with red meat but that it is only certain subtypes of red meat cooked by specific methods and/or levels of doneness that are risk factors for lung cancer. This may explain previous weaker results when looking at total meat or red meat intake, as the subgroups of meat that do not increase the risk for lung cancer may dilute the risk estimates.

For analyzing subsets of meat with very skewed distribution there are several advantages of using continuous variables rather than categorization into quantiles.[41] Due to the skewed distribution, there is little difference in the intake in lower quintiles of well-done meat. Thus, when we analyze the well-done red meat categorically the increase in risk is confined to the uppermost quantile with its large range in intake. Additional advantages are (1) the ability to directly compare odds ratios for the same amount of meat cooked in different manners, (2) looking at both addition effects adjusting for remaining red meat intake as well as substitution effects replacing one form of red meat with another, and (3) comparing results between studies.

In conclusion, we found evidence of increased lung cancer risk among the high consumers of all meat and red meat. We also found risks associated with those cooking practices that produce carcinogens such as HCAs. Further studies are warranted, especially with fewer proxy respondents and dietary questionnaires with even more detailed information on meat cooking practices. Our finding of increased risk of lung cancer with well-done and fried meat consumption needs to be viewed in context of other risk factors, such as smoking. Smoking is by far the biggest risk factor for lung cancer and cannot be minimized even when other modest risk factors are found.

Appendix I

Line item meat questions in the food frequency section of the questionnaire

Red meat items in the Questionnaire	
1.	Hamburger or cheeseburger
2.	Beef roast including on sandwiches
3.	Beef steaks including on sandwiches
4.	Pork chops or pork steaks
5.	Hot dogs or sausage
6.	Bacon
7.	Breakfast sausage
8.	Beef stew or potpie with carrots or other vegetables[a]
9.	Spaghetti, lasagna or other pasta with tomato sauce with meat[b]
10.	Liverwurst
11.	Liver, including chicken livers
12.	Ham, bologna, salami, and other lunch meats
13.	Pork roast
14.	Other ground beef including meat loaf or tacos
15.	Lamb (add on item)
White meat items in the Questionnaire	
15.	Fried chicken
16.	Any other chicken or turkey
17.	Tuna fish including salad, casserole or sandwich
18.	Fried fish or fish sandwich
19.	Other fish, not including shellfish
20.	Oysters
21.	Shellfish such as shrimp, lobster, crab, etc.
22.	Gravies made from meat drippings

[a,b] The contribution of meat in “mixed” foods were estimated, assuming 24 percent in beef stew and 9% of the total gram amount in spaghetti with meat sauce.

Appendix II

Cooking practices section

High temperature cooking methods are listed in bold face

Type of food	Method of cooking	Doneness
Hamburger or cheeseburger	Pan fried Oven broiled Grilled/barbecued Microwaved Other	Rare Medium-rare Medium Medium-well Well-done Very well-done
Beef roast	Oven roast Slow cooked such as Crock-Pot Grilled/barbecued Microwaved Other	Rare Medium-rare Medium Medium-well Well-done Very well-done
Beef steak	Pan-fried Oven broiled Grilled/barbecued Microwaved Other	Rare Medium-rare Medium Medium-well Well-done Very well-done
Fried chicken	Pan-fried Deep fried	

APPENDIX II Continued.

Type of food	Method of cooking	Doneness
Any chicken, excluding fried chicken	Stewed or boiled	Well-done
	Oven broiled	Very well-done
	Grilled/barbecued	
	Roasted or baked	
	Microwaved	
	Other	
Fried fish	Pan-fried	
	Deep fried	
Other fish, such as cod, halibut, perch, trout, excluding fried fish	Stewed or boiled	Well-done
	Oven broiled	Very well-done
	Grilled/barbecued	
	Roasted or baked	
	Microwaved	
	Other	
Pork chops or ham steaks	Pan fried	Well-done
	Oven broiled	Very well-done
	Grilled/barbecued	
	Roasted or baked	
	Microwaved	
	Other	
Hot dogs or sausage	Boiled	Well-done
	Oven broiled	Very well-done/crisp
	Grilled/barbecued	Charred
	Roasted or baked	
	Microwaved	
	Other	
Bacon	Pan-fried	Just until done
	Oven broiled	Well-done/crisp
	Microwaved	Charred
	Other	
Breakfast sausage	Pan-fried	Just until done
	Oven broiled	Well-done/crisp
	Microwaved	Charred
	Other	

Definitions of various cooking methods:
Pan fry: cooking the meat in a fry pan or on a griddle, with or without added fat.
Oven broil: cooking the meat by placing it below a heat source such as in an oven.
Grill or barbecue: cooking the meat on a grid or rack over coals, an open fire or ceramic briquettes such as those used in a gas grills.

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